Remarks. The Applicants request entry of the present amendment and reconsideration of the claims. Claims 1, 2, 14, 15, 28, 30 and 34-39 are pending. Each amended claim has written support in the specification; accordingly, no new matter has been added to the application. Each amendment to the claims and specification makes only minor, formal changes which add no new matter.

Specification informalities. The examiner alleged that the chemical formulas set forth on page 36 of the specification need correction since the proper valencies of the compounds are not set forth. The Applicants point out that the specification has been amended to insert the valencies and hereby request withdrawal of the objection.

Claim objections. The examiner objected to claims 1, 14, 28 and 30 because the chemical formulas set forth therein allegedly do not set forth the proper valencies. The proper valencies have been added to the claims. The Applicants hereby request withdrawal of the objection.

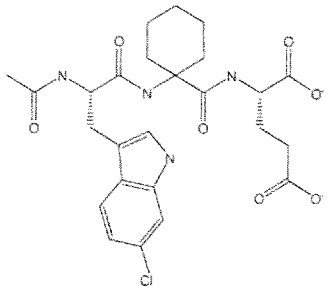
Claim rejections under 35 U.S.C. § 112(¶1)-Written Description. Claims 1, 2, 15, 28, 30, 34 and 35 stand rejected for an alleged lack of compliance with the written description requirement. The examiner alleged that the phrase "a compound represented by the structural formula" is considered to refer to a genus of compounds. The examiner stated that the Webster's Dictionary definition of the term "represent" is "to serve as a specimen, example, or instance of". The examiner explained that the instant claims have "been broadly and reasonably interpreted as encompassing a genus of compounds." The applicants disagree. The claims, with respect to the phrase at issue, do not define a genus and are fully compliant with the written description requirement.

The reasons presented by the examiner, in support of the allegation that the claims recite a genus of compounds, are

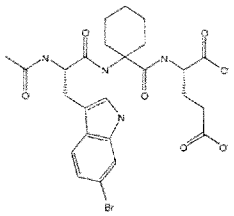
insufficient. A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, *e.g.*, *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). In this case, the examiner summarily stated that the claims have broadly and reasonably been interpreted as including a genus. A recital of the definition of "represent" was also made, however, how this definition, somehow, justifies finding the claim to recite a genus of compounds is not explained. Indeed, the examiner's justification for this finding makes it impossible for the applicants to adequately evaluate it. For example, it is unclear how the Webster's definition of "represent" (*i.e.*, "to serve as a specimen, example, or instance of") could justify this claim interpretation. There is nothing in the common usage of the words "represent", "specimen", "example" or "instance" which would support the examiner's claim interpretation. The applicants hereby request more explanation of the basis on which the claims have been rejected.

Furthermore, the Court of Appeals for the Federal Circuit, sitting *en banc*, in the recent case of *Phillips v. AWH Corp.*, cautioned against resorting exclusively to dictionary definitions, in place of the specification, when construing claim language. 415 F.3d 1303 (Fed. Cir. 2005). In this case, the examiner appears to have done just that. There was no reasoning, in the rejection, based on the teachings of the specification which would justify the examiner's claim construction. Indeed, there *is* nothing in the specification which would support the rejection.

In any event, the chemical formulae at issue are



and



. A practitioner of ordinary skill in the art would not consider these formulae as describing genuses because variable substituents are not included. Typically, chemical genuses are described using variable substituents.

The claims has been amended to delete the term "soluble". Although the claims were amended in the response submitted previous to this response, Applicants have reconsidered the issue and believe that inclusion of this term is unwarranted. The written description issues raised in the present office action and in the previous office action are addressed herein.

The applicants submit that claims 1, 2 and 15, as amended, are compliant with the written description requirement at least for the reasons set forth herein; including the relevant case law concerning the written description requirement, the USPTO Written Description Guidelines and USPTO comments of official Patent Office examination policy made in connection with the Trilateral Project.

The examiner took the position that the claims, which recite a "purified polypeptide", comprise crystalline and non-crystalline, soluble polypeptides. Further the examiner took the position that the specification has only exemplified a

single crystal and, so, the full scope of the claimed subject matter has not been described. The examiner stated, in a subsequent telephone interview with the undersigned (held on June 18, 2007), that limiting the claims to "soluble" polypeptides would make the claims compliant with the written description requirement. In the present office action, the examiner indicates that the claims should recite "non-crystalline" polypeptides in order to comply with the written description requirement.

The applicants agree that the claims, as amended, broadly include all polypeptides, crystalline and non-crystalline alike. The applicants do not agree that other crystalline polypeptides must be exemplified in order to provide a sufficient description of the full scope claims to comply with the requirement. Rather, description of the amino acid sequence of the claimed polypeptides is a sufficient description.

The case law arising out of the Court of Appeals for the Federal Circuit ("Federal Circuit") provides robust support for the argument that the amended claims are compliant with the written description requirement.

The Federal Circuit case of *Fiers v. Revel*, as applied in *Regents of University of California v. Eli Lilly & Co.* provides the first line of support for this argument. 984 F.2d 1164 (Fed. Cir. 1993); 119 F.3d 1559 (Fed. Cir. 1997)

In *Fiers v. Revel*, the Federal Circuit held that the nucleotide sequence of a claimed DNA molecule constitutes adequate written description. 984 F.2d at 1170. In *Fiers*, an issue was whether appellee-Sugano was entitled to his March 18, 1980 Japanese priority date concerning a patent application covering DNA encoding interferon. *Id.* at 1166-1168. The *Fiers* Court held that Sugano was entitled to his filing date since he had satisfied the written description

requirement with regard to the claimed DNA as of March 18, 1980. Specifically, the Court found that, as of this date, Sugano had provided a complete sequence for the claimed molecule. The *Fiers* Court stated as follows:

> We also conclude that Sugano's application satisfies the written description requirement since it sets forth the complete and correct nucleotide sequence of a DNA coding for B-IF and thus "convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, [Sugano] was in possession of the [DNA coding for B-IF].

Id. at 1172 (Fed. Cir. 1993) (quoting *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)).

Fiers relates to the description of DNA and not protein, however, its holding can clearly be applied to the instant case. Both DNA and protein are polymeric molecules, composed of a limited number of types of subunits, which are capable of crystallization and yielding structural data. Indeed, the helical structure of DNA was discovered by Watson and Crick on the basis of X-ray diffraction data gotten from crystallized DNA. Furthermore, if a DNA sequence is known, the encoded amino acid sequence would also be easily identifiable from this information. So, it follows that if a DNA encoding B-IF is sufficiently described by its nucleotide sequence, then its encoded B-IF amino acid sequence, which is directly derivable therefrom, would also be sufficiently described (had it been claimed). Thus, the amount of written description relating to claims covering DNA and claims covering protein should be somewhat similar. Indeed, the *Fiers* court made no mention of the need to limit the claims at issue to non-crystalline molecules in order to comply with the written description requirement.

Later, *Fiers* was cited in the holding of the case of *Regents of University of California v. Eli Lilly & Co.* In *Lilly*, the Federal Circuit addressed whether claims in a patent, owned by the Regents of the University of California, directed to cDNA encoding insulin, were sufficiently described. *Regents of University of California*, 119 F.3d at 1562 (Fed. Cir. 1997). The Court found the claims invalid because the cDNA was not sufficiently described. *Id.* In making this finding, the Court exemplified what is necessary for cDNA to be sufficiently described. The Court, referring to *Fiers*, stated that compliance with the requirement "requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the DNA." *Id.* at 1569. Again, the Court did not state that the claims must recite the nucleotide sequence and exclude crystalline molecules. As was discussed above, this holding should apply equally to the amino acid sequence of a claimed polypeptide notwithstanding the fact that the case dealt with DNA. Requiring the instant claims to be so limited, in the interest of finding them compliant with the written description requirement, would not be justified.

A further relevant case from the Federal Circuit is *Invitrogen Corp. v. Clontech Labs., Inc.* 429 F.3d 1052 (Fed. Cir. 2005). In this case, the Court examined whether a patent owned by Invitrogen directed to a polypeptide with DNA polymerase activity was compliant with the written description requirement. *Id.* at 1057-1060. A claim pointed out by the Court was as follows:

> 1. An isolated polypeptide having DNA polymerase activity and substantially reduced RNase H activity, wherein said polypeptide is encoded by a modified reverse transcriptase nucleotide sequence that encodes a modified amino acid sequence resulting in said polypeptide having

> substantially reduced RNase H activity, and wherein said nucleotide sequence is derived from an organism selected from the group consisting of a retrovirus, yeast, Neurospora, Drosophila, primates and rodents.

Id. at 1072.

The specification provided an amino acid sequence and related sequences were known in the art. *Id.* at 1073. The Court found the claims to be sufficiently described, in part, because "the shared written description for the patents-in-issue recites both the DNA and amino acid sequences of a representative embodiment of the claimed RT enzyme." *Id.* Here, the Court found the claimed polypeptides to be sufficiently described on the basis of disclosure of amino acid sequence data. There was no mention of the need to limit the claims to non-crystalline polypeptides. Accordingly, the instant claims should not need to be so limited in order to comply with the written description requirement.

Furthermore, as mentioned above, the USPTO Written Description Guidelines and the Office's expressions of official policy in reports of the Trilateral Project further substantiate the point that the amended claims are fully described without inclusion of the non-crystalline limitation.

Example 13 of the Written Description Guidelines considers a hypothetical claim:

> 1. An isolated protein having SEQ ID NO: 3.

; wherein the hypothetical specification discloses the SEQ ID NO: 3 amino acid sequence. The Guidelines state that the claim is compliant with the written description requirement. The Guidelines do not state that the claims should be limited to non-crystalline polypeptides in order to be compliant. Likewise, the instant application discloses all amino acid

sequences specified in the claims and should, similarly, be deemed compliant.

In addition, the Trilateral Project "Report on Comparative Study on Biotechnology Patent Practices Carried Out Under Trilateral Project B3b" further substantiates the argument that the instant claims, as amended, are compliant with the written description requirement. In example 1 of "Annex 1: Comments of the USPTO", the USPTO discusses an application with the hypothetical claim:

> 1. An isolated and purified receptor the sequence of which consists of SEQ ID NO: 1.

The hypothetical specification discloses the amino acid sequence of SEQ ID NO: 1. The USPTO found the claimed polypeptide sufficiently described simply because the amino acid sequence was disclosed. Specifically, the USPTO stated:

> This claim meets the requirement for an adequate written description of the claimed invention because the scope of the claim is limited to a protein molecule whose primary structure is specifically disclosed.

The USPTO made no mention of any need to exclude crystalline receptors from the claim scope.

More support for the argument that the amended claims are sufficiently described comes from Comments of the USPTO on Trilateral Project WM4, "Comparative study on protein 3-dimensional (3-D) structure related claims". In case 5 of the USPTO comments, the hypothetical applicants sought the following two claims:

> Claim 1: An isolated and purified molecule comprising a binding pocket of protein P defined by the structural coordinates of amino acid residues 223, 224, 227, 295, 343, 366, 370, 378 and 384 according to Figure 1.

> Claim 2: An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO: 1.

These claims are directed to an isolated and purified polypeptide with no limitation as to its crystalline or non-crystalline status. In the background of the hypothetical application, the applicants had X-Ray diffraction data on the protein:

> -The description teaches that the possible peptides that begin with any amino acid from position 214 to 218 and end with any amino acid from position 394 to 401 of SEQ ID NO: 1 are protein domains that are able to fold into an active binding pocket of protein P. This ability was confirmed by X-ray diffraction data. (emphasis added).

Thus, the hypothetical applicants must have crystallized the protein and discussed it in the specification. The USPTO stated that claim 2 was compliant with the written description requirement. Claim 1 was not compliant for reasons unrelated to the basis on which the present claims are rejected. The USPTO made no statement that the claimed polypeptide would need to be limited to non-crystalline polypeptides in order to be compliant. Similarly, putting such a requirement on the present claims would not be proper.

During the June 18, 2007 telephone interview, the examiners expressed doubt as to whether the Guidelines and Trilateral Agreement documents were applicable to the instant case since the examples cited in support of this point do not explicitly discuss crystals. Specifically, in the examiners' interview summary, the following was stated:

> The examiners noted there is no indication in the facts provided for Example 13 of the

> Guidelines that the claims are intended to encompass protein crystals of the polypeptide.

This counter-point is refuted by the USPTO comments to "Comparative study on protein 3-dimensional (3-D) structure related claims" which is discussed above. In the comments, protein crystals *are* discussed in terms of X-ray diffraction data. Aside from this, the examiner's argument is not well founded because it conflicts with jurisprudence concerning proper claim interpretation. In general, claims are to be "given their broadest reasonable interpretation consistent with the specification". *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005). Further explaining claim interpretation, the Federal Circuit, in *Liebel-Flarsheim Co. v. Medrad, Inc.*, clearly favored broad interpretation of claim language. 358 F.3d 898 (Fed. Cir. 2004). In *Liebel-Flarsheim*, the Court found that, although the specification discussed various embodiments of the claimed invention, it would be improper to exclude other embodiments only because they were not specifically discussed. *Id.* at 909. Specifically, the *Liebel-Flarsheim* Court stated:

> absent a clear disclaimer of particular subject matter, the fact that the inventor may have anticipated that the invention would be used in a particular way does not mean that the scope of the invention is limited to that context

Id. (citing *Northrop Grumman Corp. v. Intel Corp.*, 325 F.3d 1346, 1355 (Fed. Cir. 2003)).

Clearly, none of the hypothetical examples discussed above mention any such disclaimer of crystals; and, so, the corresponding hypothetical claims should be interpreted as including crystals. Moreover, none of the case law discussed above made any mention, whatsoever, of any disclaimer of crystalline polypeptides or DNA in the claims that were at

issue. Thus, the Court would have regarded the claims at issue, in each case, as including crystals. The examiner's contention that, simply because crystals were not specifically mentioned in the Guidelines example, crystals would not be encompassed by the hypothetical claim is not in accord with the law of claim interpretation.

In view of claim construction law, an implication of the examiner's contention, that only polypeptide claims supported by specifications disclosing crystals will be interpreted to encompass crystals, would be contrary to U.S. patent policy. Patent policy is based on encouragement of the full and early disclosure of one's invention in exchange for a limited monopoly on the invention. Thus, in a case where only a single crystal was made, the applicant would be more likely to obtain broader claims by withholding information regarding the single crystal than by disclosing the information. If no crystal were disclosed, there would be no need to limit the claims to non-crystalline polypeptides. Such a policy, by encouraging the withholding of information, would be contrary to patent policy.

The examiners further argued that the examination policy behind the rejection of the instant claims was discussed with a Technology Quality Assurance Specialist and presented in a Biotech Customer Partnership meeting. The applicants submit that the weight of case law and USPTO policy evidence presented herein outweighs whatever probative value the discussions the examiner had with the Specialist and at the Partnership meeting. Indeed, exactly what was stated at these events was not made of record and cannot fairly be used as any grounds on which to base any claim rejection. See *e.g.*, *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971).

During the June 18, 2007 telephone interview, the examiners argued that the Written Description Guidelines are

only that, guidelines, which need not necessarily be followed in every case. This line of argument was not committed to writing in the interview summary. The Applicants submit that, in the absence of any particular purpose for deviating from the provisions of the Guidelines, to do so would be improper. In the instant case, no such reason has been given and, accordingly, deviation from the Guidelines is improper.

The claims as amended are fully compliant with the written description requirement. The Applicants request withdrawal of the rejection.

Claim rejections under 35 U.S.C. § 112(¶1)-Enablement. Claims 1, 2 and 15 stand rejected as allegedly lacking sufficiently enabling support. The applicants submit that the claims, as amended, are fully enabled and that rejection of the claims for lack of enablement is not and would not be proper. The enablement requirement, with respect to a polypeptide, is met by description of the amino acid sequence of the polypeptide. This is regardless of whether the specification discusses crystals.

As is discussed herein, the claims encompass the specified polypeptide in any form, including crystalline and non-crystalline forms. The specification teaches how to make and use a particular crystal (see *e.g.*, example 2). A practitioner of ordinary skill in the art could easily use this disclosure as a guide to screen additional crystallization conditions for making additional crystals. Indeed, the art of protein crystallization makes such high throughput screening of crystallization conditions, particularly automated screening, convenient. Any practitioner of ordinary skill in the art would appreciate this point. Assuming, *arguendo*, that the specification does not enable the production of such additional crystals, this is

not fatal with respect to the enabled status of the claims. As noted in the M.P.E.P. § 2164.08:

> the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). (emphasis added).

This passage indicates that an applicant need not exhaustively disclose how to make and use each and every embodiment of the invention within the claim scope. If the number of embodiments enabled is reasonably correlated with the claim scope, then this is sufficient. Even if the specification does not enable production of every last crystal, the specification enables a scope of subject matter which bears a reasonable correlation to the scope of the claims. The scope of the claims includes, for example, not only crystals, but also soluble polypeptides, fusions thereof and complexes thereof. All of these embodiments are enabled. The examiner is giving undue weight to the number of crystals of the claimed protein encompassed by the claims while ignoring the other embodiments which are also encompassed.

The USPTO expression of the enablement requirement set forth in M.P.E.P. § 2164.08 is applied in several different sources which are discussed *infra*. The examiner's attention is directed, for example, to the Comments of the USPTO on Trilateral Project WM4, "Comparative study on protein 3-dimensional (3-D) structure related claims". These Comments were discussed above, in connection with the written description requirement. The two hypothetical claims were:

> Claim 1: An isolated and purified molecule comprising a binding pocket of protein P defined by the structural coordinates of amino acid residues 223, 224, 227, 295, 343, 366, 370, 378 and 384 according to Figure 1.

> Claim 2: An isolated and purified polypeptide consisting of a portion of protein P starting at one of amino acids 214 to 218 and ending at one of amino acids 394 to 401 of protein P as set forth in SEQ ID NO: 1.

The background of the hypothetical application stated:

> -The description teaches that the possible peptides that begin with any amino acid from position 214 to 218 and end with any amino acid from position 394 to 401 of SEQ ID NO: 1 are protein domains that are able to fold into an active binding pocket of protein P. This ability was confirmed by X-ray diffraction data. (emphasis added).

Again, the applicants must have crystallized the protein and discussed it in the specification. In the discussion of the enablement requirement that followed, there was no mention, whatsoever, of a need to limit the claims to non-crystalline polypeptides. Indeed, the discussion found that "[w]ith respect to the enablement requirement, the specification enables the full-length protein P and the specifically disclosed fragments." Moreover, claim 2 was compliant with the enablement requirement. The USPTO comments stated:

> Claim 2 complies with the enablement and written description requirements because it is limited to fragments of protein P that contain the binding pocket and were shown in the specification to retain binding activity and the signaling activity of protein P.

Further support for this position may be found in the M.P.E.P. at § 2164.08 wherein the following is stated:

> However, when claims are directed to any purified and isolated DNA sequence encoding a specifically named protein where the protein has a specifically identified sequence, a rejection of the claims as broader than the

> enabling disclosure is generally not appropriate because one skilled in the art could readily determine any one of the claimed embodiments. (emphasis added)

The instant claims relate to polypeptides and not DNA, however, as is discussed above, the policy behind this statement lends support to the proposition that the claims, as amended, are enabled without the addition of a "non-crystalline" limitation. If it would not be proper to reject a claim covering a DNA encoding a known protein sequence, it similarly should not be proper to reject a claim covering the protein.

The "Training Materials for Examining Patent Applications with Respect to 35 USC Section 112, First Paragraph-Enablement of Chemical/Biotechnical Applications", which is available on the USPTO website (www1.uspto.gov/go/pac/dapp/1pecba.htm#7e) lends additional support for the argument that the amended claims are enabled in the absence of a "non-crystalline" limitation. Example 5E, of the Training Materials, discusses a hypothetical claim:

> 1. A peptide consisting of the sequence
>
> Phe Ile Gly His Thr Ser Xaa Thr His Glu Xaa Phe Ala Thr Xaa Trp Glu Leu Leu (SEQ ID No. 1), wherein
>
> Xaa at position 7 is Gln, Ile, or Met;
> Xaa at position 11 is Asp, Gln, or Glu; and
> Xaa at position 15 is Ser or Pro

wherein the specification teaches how to make such polypeptides.

The Training Materials parses the enablement requirement into two elements-"how to use", which is reflected in the Utility requirement; and "how to make" (the grounds on which the instant claims are rejected). The discussion states that

the "how to make" element of enablement is "not an issue". There is no mention that the polypeptide specified in the claims should be limited to a non-crystalline polypeptide in spite of the fact that such claims would cover crystalline polypeptides (see discussion of claim construction law above). In the instant rejection, the enablement issue is that the specification allegedly does not teach how to make the claimed polypeptides. Similar to the hypothetical claim, how to make the claimed polypeptides should not be an issue.

Withdrawal of the claim rejections is appropriate and the Applicants request such action.

Conclusion.

The claims are in condition for passage to allowance. Such action is earnestly solicited. The examiner is invited to contact the undersigned should there be any outstanding questions or concerns regarding the present application.

Respectfully submitted,

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